response accuracy, that was accompanied by an increase in response latencies only. These results provide addnl. support for the involvement of cholinergic, rather than dopaminergic mechanisms in short-term memory processes supported by the medial PFC of the rat, and they are not in favor of a functional dissocn. between the dorsomedial PFC and the ventromedial PFC in this role.

AN 1995:433975 CAPLUS
DN 122:205805
TI The role of the medial prefrontal cortex of rats in short-term memory functioning: further support for involvement of cholinergic, rather than dopaminergic mechanisms
AU Broersen, Laus M.; Heinsbroek, Rob P. W.; Bruin, Jan P. C. de; Uylings, Harry B. M.; Olivier, Berend
CS Graduate School Neurosciences Amsterdam, Netherlands Institute for Brain Research, Meibergdreef 33, 1105 AZ, Amsterdam, Neth.
SO Brain Res. (**1995**), 674(2), 221-9
CODEN: BRREAP; ISSN: 0006-8993
DT Journal
LA English
TI The role of the medial prefrontal cortex of rats in short-term memory functioning: further support for involvement of cholinergic, rather than dopaminergic mechanisms
SO Brain Res. (**1995**), 674(2), 221-9
CODEN: BRREAP; ISSN: 0006-8993
AB The putative involvement of the dopaminergic innervation of the medial part of the prefrontal cortex (PFC) in short-term memory functioning was investigated by evaluating the effects of local infusions of dopaminergic drugs into the ventral part of the medial PFC of rats in an operant delayed-matching-to-position (DMTP) task. Two sep. groups of rats were tested after bilateral microinfusion of several doses of either the dopamine receptor agonist **apomorphine** (APO) or the dopamine receptor antagonist cis-flupenthixol (FLU) into the ventromedial PFC. In addn., all animals were tested after infusion of several doses of the muscarinic receptor antagonist scopolamine (SCO) and the dopamine D1 receptor antagonist SCH 23390 (SCH). The drugs tested affected DMTP performance differentially. APO had no effect on response accuracy, although it dose-dependently affected **nose** poke activity and response latencies. FLU and SCH both induced a dose-dependent, but delay-independent deterioration of response accuracy that was paralleled by increases in response latencies and decreases in **nose** poke frequencies, causing some animals to stop responding after infusion of the highest doses of both drugs. In contrast, SCO infusions into the ventromedial PFC induced a dose- and delay-dependent deterioration of response accuracy, that was accompanied by an increase in response latencies only. These results provide addnl. support for the involvement of cholinergic, rather than dopaminergic mechanisms in short-term memory processes supported by the medial PFC of the rat, and they are not in favor of a functional dissocn. between the dorsomedial PFC and the ventromedial PFC in this role.

L5 ANSWER 10 OF 29 SCISEARCH COPYRIGHT 2002 ISI (R)
AB Objectives. **Apomorphine** has been reported to be effective in causing erections in animals and man when administered parenterally. The

[redacted]

side effects, notably nausea, have seriously limited its clinical usefulness. We formulated **apomorphine** for controlled sublingual absorption and herein report on four preliminary studies evaluating efficacy and side effects in men with no documentable organic cause of erectile dysfunction.

Methods. Patients complaining of erectile dysfunction underwent a careful evaluation. Those with measurable organic dysfunction or known organic factors were excluded. Men with primarily psychogenic impotence were tested with one of four protocols of an **apomorphine** preparation (preliminary sublingual liquid, preliminary 5 mg tablet, aqueous **nasal** spray, and new 3 and 4 mg controlled absorption tablets). The erectile response of these men to the drug with visual erotic or sexually neutral stimulation was studied with the Rigiscan.

Results. Seven of 10 evaluable patients responded to the sublingual liquid preparation but the majority experienced significant nausea. The preliminary 5 mg tablet and aqueous forms did not produce useful responses free of side effects. The newly formulated controlled absorption 3 and 4 mg tablets were tested in 12 men. Eight of 12 (67%) developed erections in response to **apomorphine**. Erectile activity was seen during sexually neutral visual stimulation to a significantly greater extent than with placebo. Home trial use was found to be successful and sustained by 7 of 11 (64%) patients.

Conclusions. We have shown that **apomorphine** will act as an erectogenic agent when absorbed through the oral mucosa. in a carefully selected group of impotent patients with no documentable organic causes of erectile dysfunction, but with proven erectile potential, 67% will experience significantly durable erections with a dose of 3 or 4 mg of **apomorphine** when formulated for controlled absorption. The results in these small groups appear to justify larger clinical studies of this proprietary formulation.

AN 95:128992 SCISEARCH
GA The Genuine Article (R) Number: QF117
TI RECOVERY OF ERECTILE FUNCTION BY THE ORAL-ADMINISTRATION OF APOMORPHINE
AU HEATON J P W (Reprint); MORALES A; ADAMS M A; JOHNSTON B; ELRASHIDY R
CS QUEENS UNIV, DEPT UROL, KINGSTON, ON, CANADA (Reprint); QUEENS UNIV, DEPT PHARMACOL & TOXICOL, KINGSTON, ON K7L 3N6, CANADA; QUEENS UNIV, HUMAN SEXUAL GRP, KINGSTON, ON, CANADA; PENTECH PHARMACEUT, WHEELING, IL, 00000
CYA CANADA; USA
SO UROLOGY, (**FEB 1995**) Vol. 45, No. 2, pp. 200-206.
ISSN: 0090-4295.
DT Note; Journal
FS CLIN
LA ENGLISH
REC Reference Count: 20
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
TI RECOVERY OF ERECTILE FUNCTION BY THE ORAL-ADMINISTRATION OF APOMORPHINE
SO UROLOGY, (**FEB 1995**) Vol. 45, No. 2, pp. 200-206.
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AB Objectives. **Apomorphine** has been reported to be effective in

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causing erections in animals and man when administered parenterally. The side effects, notably nausea, have seriously limited its clinical usefulness. We formulated **apomorphine** for controlled sublingual absorption and herein report on four preliminary studies evaluating efficacy and side effects in men with no. . . or known organic factors were excluded. Men with primarily psychogenic impotence were tested with one of four protocols of an **apomorphine** preparation (preliminary sublingual liquid, preliminary 5 mg tablet, aqueous **nasal** spray, and new 3 and 4 mg controlled absorption tablets). The erectile response of these men to the drug with. . . absorption 3 and 4 mg tablets were tested in 12 men. Eight of 12 (67%) developed erections in response to **apomorphine**. Erectile activity was seen during sexually neutral visual stimulation to a significantly greater extent than with placebo. Home trial use was found to be successful and sustained by 7 of 11 (64%) patients.

Conclusions. We have shown that **apomorphine** will act as an erectogenic agent when absorbed through the oral mucosa. in a carefully selected group of impotent patients. . . but with proven erectile potential, 67% will experience significantly durable erections with a dose of 3 or 4 mg of **apomorphine** when formulated for controlled absorption. The results in these small groups appear to justify larger clinical studies of this proprietary. . .

L5 ANSWER 11 OF 29 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 9

AB We present a review of the recent literature and personal experience with **apomorphine** in patients with Parkinson's disease.

Apomorphine is a potent D1 and D2 dopaminergic agonist. It has a rapid and short duration effect after subcutaneous administration at doses ranging from 15 to 180 .mu.g/kg. Plasma maximal concentration is reached in 8-16 minutes, with a plasma half life of 34-70 minutes. Bioavailability is close to 100%. Repeated injections in patients show post-stimulative hyposensitivity. **Apomorphine** lest appears very useful for the differential diagnosis between idiopathic Parkinson's disease and other Parkinson plus syndromes, and as a predictive test for dopaminergic responsiveness. Appropriate doses are able to alleviate akinesia, rigidity and tremor. Recent therapeutic trials have demonstrated the high interest of intermittent multiple subcutaneous **apomorphine** injections to cut tile 'off' motor phases in fluctuating parkinsonian patients under chronic levodopa treatment. In some cases, continuous **apomorphine** subcutaneous infusion with a portable pump may be required, particularly when levodopa treatment is temporarily interrupted, as after abdominal surgery. During long-term treatment, the **apomorphine** dose able to relieve akinesia remains stable. Peripheral side effects such as nausea and hypotension may be prevented by the co-administration of domperidone, a peripheral dopaminergic antagonist. Cutaneous fibrous nodules and psychiatric symptoms may occur, but usually at high dosages with continuous infusion. Local allergic effects have limited the use of other routes of administration, such as **intranasal**, sublingual, and rectal routes. **Apomorphine** is also used as a pharmacological

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L4 ANSWER 5 OF 81 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:121778 BIOSIS
DN PREV199799428281
TI **Nasal** spray vs. oral administration of **bromocriptine**: Pharmacology and effect on serum prolactin in puerperal women.
AU Cicinelli, E. (1); Cignarelli, M.; Petruzzi, D.; Matteo, M. G.; Ruccia, C.; Schonauer, L. M.
CS (1) Via Addis Abeba 21, 70121 Bari Italy
SO Journal of Endocrinological Investigation, (1996) Vol. 19, No. 7, pp. 427-432.
ISSN: 0391-4097.
DT Article
LA English
AB The oral administration of **bromocriptine** induces a variety of side-effects in about 50-70% of patients, the most common being nausea and vomiting, probably related to the local gastrointestinal effect of the drug. **Nasal** administration makes it possible to avoid intestinal and liver metabolism. This study compared the serum concentrations of **bromocriptine** and prolactin (PRL) in twenty puerperal women who had asked to discontinue breast feeding and were randomized to receive a single oral (2.5 mg) or **nasal** spray dose (0.8 mg) of **bromocriptine**. Serum **bromocriptine** and PRL concentrations were measured at various times before and after drug administration. At 15 min, the circulating concentrations of **bromocriptine** were about eight times higher after **nasal** than after oral administration; peak serum concentration (CMax) was reached respectively 45 min and 60 min after administration, and was about three times higher after **nasal** administration (314+-102 pg/ml vs 112.30+-34.47 pg/ml). The reduction in serum PRL concentrations was also more rapid in the **nasally**-treated group reaching the normal assay range of lt 20 mu-g/l within two as against five hours post-administration. Four orally-treated patients complained of nausea; in the **nasally**-treated group, six patients reported only a mild endonasal burning that disappeared within a few minutes of administration.
Our results suggest that the **nasal** administration of **bromocriptine** may lead to a reduction in the required overall dose and fewer gastrointestinal side-effects, and may therefore improve therapy compliance.
CC Pathology, General and Miscellaneous - Therapy 12512
Metabolism - Metabolic Disorders *13020
Endocrine System - Pituitary *17014
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
Pharmacology - Clinical Pharmacology *22005
Pharmacology - Endocrine System *22016
Routes of Immunization, Infection and Therapy *22100
Toxicology - Pharmacological Toxicology *22504
BC Hominidae *86215
IT Major Concepts

[redacted]

[redacted]

Endocrine System (Chemical Coordination and Homeostasis); Metabolism; Methods and Techniques; Pharmacology; Toxicology

IT Chemicals & Biochemicals

BROMOCRIPTINE; PROLACTIN; DOPAMINE

IT Miscellaneous Descriptors

BROMOCRIPTINE; CLINICAL ENDOCRINOLOGY; DOPAMINE RECEPTOR AGONIST-DRUG; FEMALE; GASTROINTESTINAL SIDE EFFECTS; HYPERPROLACTINEMIA; METABOLIC DISEASE; **NASAL** SPRAY ADMINISTRATION; ORAL ADMINISTRATION; PATIENT; PHARMACOKINETICS; PHARMACOLOGY; PROLACTIN

ORGN Super Taxa

Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

human (Hominidae)

ORGN Organism Superterms

animals; chordates; humans; mammals; primates; vertebrates

RN 25614-03-3 (**BROMOCRIPTINE**)
9002-62-4 (PROLACTIN)
51-61-6 (DOPAMINE)

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